## REMARKS

The Office Action of June 24, 2004, has been received and reviewed. Claims 1, 3-11, 14-16, 18 and 21-25 are currently pending in the application, and all pending claims stand rejected. Claims 1, 5, 7-8, 10-11, 15, 18 and 21-24 have been amended and new claims 26-27 have been added as set forth herein. All amendments and cancellations are made without prejudice or disclaimer. Reconsideration is requested.

**Objection to Abstract**

The abstract of the disclosure was objected to because of the presence of typed materials which are not related to the disclosure. The Abstract has been amended to comply with the requirements of MPEP § 608.01(b). Withdrawal of the objection is requested.

**Rejections under 35 U.S.C. § 112, second paragraph**

Claims 11, 16, 24 and 25 stand rejected under 35 U.S.C. § 112, second paragraph, as assertedly being indefinite. Claims 16 and 25 have been canceled rendering the rejections thereof moot. Applicants respectfully traverse the remaining rejections.

It was thought that the steps in the methods of claims 11 and 24 were indefinite for not achieving the goal set forth in the claim preambles. Although applicants do not agree that any of the claims are indefinite, to expedite prosecution, claims 11 and 24 have been amended as set forth herein.

Specifically, with regard to claim 11, it was thought that a step of determining or measuring binding was missing. As amended, claim 11 recites in part "selecting cells in which the cell's recombinant reporter system is inactivated." Thus, amended claim 11 should be clear since determining or measuring binding is ascertained by the inactivation of the recombinant reporter system. For instance, if the cell's recombinant reporter system is inactivated, then the binding of the ligand with the extracellular part of the chimeric receptor is inhibited by the compound, or the signaling pathway of the cytoplasmic part of the chimeric receptor is inhibited. Further, claim 11 has been amended to recite "thereby identifying" in accordance with the suggestion of the Examiner. Thus, amended claim 11 should be definite.

With regard to claim 24, it was thought to be unclear how an antagonist could be identified by determining the ability of the compound to activate the reporter system. Although applicants do not agree that claim 24 is indefinite, to expedite prosecution, claim 24 has been amended to recite in part contacting said mammalian cell with a possible antagonist; and selecting mammalian cells in which said recombinant reporter system is inactivated; thereby identifying an antagonist of the chimeric receptor and to remove the recitation of "a positive or a negative control." Thus, amended claim 24 should be definite since an antagonist of the chimeric receptor would be identified by inactivation of the recombinant reporter system and selection of the cell having the inactivated recombinant reporter system.

Reconsideration and withdrawal of the indefiniteness rejections of claims 11 and 24 are requested.

**Rejections under 35 U.S.C. § 103**

Claims 1, 3-6, 10, 11, 14-16, 18 and 21-25

Claims 1, 3-6, 10, 11, 14-16, 18 and 21-25 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Pestka et al. in view of Trueheart et al. Claims 16 and 25 have been canceled rendering the rejections thereof moot. Applicants respectfully traverse the remaining rejections.

Although applicants do not agree that a *prima facie* case of obviousness has been established with regard to any of the rejected claims and reassert remarks made in previous amendments, to expedite prosecution, claim 1 has been amended. Amended claim 1 is directed to a mammalian cell comprising a first recombinant gene encoding a chimeric receptor comprising an extracellular domain of a first receptor fused to a cytoplasmic domain of a second receptor capable of inducing a recombinant reporter system and a recombinant reporter system that is activated or inactivated upon the creation of said autocrinic or anti-autocrinic loop.

A *prima facie* case of obviousness cannot be established with regard to amended claim 1 since the cited references do not alone, or in combination, teach or suggest each and every element of amended independent claim 1. For instance, Pestka et al. does not teach or suggest a cell having first recombinant gene encoding a chimeric receptor having a cytoplasmic domain of a second receptor capable of inducing a recombinant reporter system or a cell having a

recombinant reporter system. Rather, Pestka et al. discloses "detection of IL-10 receptor-mediated activation (or inhibition of activation) can be accomplished by evaluating changes in cell targets ... by detecting increased phosphorylation of Tyk2, activation of Stat1 or Stat3, decreased production of interferon-γ." (Pestka et al., pages 36-37). Thus, Pestka et al. relies on the natural response of the cell that signals the cytoplasmic part of the receptor of Pestka et al. and not a recombinant reporter system.

A resultant combination of Trueheart et al. with Pestka et al. also does not establish a *prima facie* case of obviousness since Trueheart et al. also does not teach or suggest a cell having a first recombinant gene encoding a chimeric receptor having a cytoplasmic domain of a second receptor capable of inducing a recombinant reporter system or a cell having a recombinant reporter system as recited in amended claim 1. As stated in Trueheart et al. "in a preferred embodiment, the step of measuring comprises measuring the transcription of an **endogenous** gene or the activity of an **endogenous** protein in the cell" which is not recombinant. (Trueheart et al., page 7) (emphasis added). Thus, the cited references do not alone, or in combination, teach or suggest each and every element of amended claim 1 as required for obviousness.

Each of independent claims 15 and 24 have also been amended and are directed to, *inter alia*, providing a mammalian cell comprising a first recombinant gene encoding a chimeric receptor comprising an extracellular domain of a first receptor fused to a cytoplasmic domain of a second receptor capable of inducing a recombinant reporter system, and a mammalian cell having a recombinant reporter system that is activated upon the creation of said autocrinic loop. As previously established herein, the resultant combination of Pestka et al. with Trueheart et al. does not result in a teaching or suggestion of a receptor capable of inducing a recombinant reporter system or the recombinant reporter system as required to establish obviousness.

Further, no suggestion or motivation exists to combine the disclosure of Pestka et al. with Trueheart et al. Pestka et al. does not describe any screening system and, thus, one of ordinary skill in the art would not be motivated to modify Pestka et al. or combine Pestka et al. with Trueheart et al. in order to arrive at the mammalian cell of claim 1, the method for identifying an agonist as recited in amended claim 15 or the method for identifying an antagonist as recited in amended claim 24. Rather, Pestka et al. intended to develop an assay system for a given cytokine (*See*, Pestka et al. at page 8, line 23 and page 10, lines 25-26) or to reconstitute responsiveness to

a soluble factor (*See, Id.* at page 10, line 28). In either instance, Pestka et al. starts with a well known ligand, not a complex mixture of unknown compounds. Thus, no suggestion or motivation exists to combine the cited references.

With regard to the statement in the Office Action indicating

> the Examiner notes that Applicants' argument is equivalent to argue that the instantly claimed invention is not enabled in its full scope because the instant claims are drawn to a mammalian cell comprising a chimeric receptor or a screening method of using the cell, whereas a chimeric receptor encompasses any chimeric receptors, e.g., GPCRs

(Office Action, page 8), the applicants point out that the pending claims are enabled and do not agree with the statement in the Office Action. Rather, the statement in the Office Action appears to be an impermissible hindsight reconstruction of the applicants' invention in order to formulate obviousness.

Since dependent claims 3-6, 10, 11, 14, 18 and 21-23 include the elements of independent claim 1 or 15 and a *prima facie* case of obviousness cannot be established with regard to independent claim 1 or 15, a *prima facie* case of obviousness also cannot be established with regard to any of dependent claims 3-6, 10, 11, 14, 18 and 21-23.

Reconsideration and withdrawal of the obviousness rejections of claims 1, 3-6, 10, 11, 14-15, 18 and 21-24 are requested.

Claims 7 and 8

Claims 7 and 8 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Pestka et al. in view of Trueheart et al., and further in view of Pelligrini et al. Applicants respectfully traverse the rejections.

Since dependent claims 7 and 8 include the elements of independent claim 1 and a *prima facie* case of obviousness cannot be established with regard to independent claim 1, a *prima facie* case of obviousness also cannot be established with regard to dependent claims 7 and 8.

Further, a *prima facie* case of obviousness cannot be established with regard to claims 7 and 8 since one of ordinary skill in the art would not have a reasonable expectation of success in combining the cited references. Since the claimed invention must be considered as a whole in determining the differences between the cited reference and the claimed invention (*See,* MPEP §

2141.01), one of ordinary skill in the art would not reasonably expect to be able to detect the IL-10 receptor-mediated activation of Pestka et al. with the *E. coli* xanthine-guanine phosphoribosyl transferase (gpt) of or the 6-16 reporter of Pelligrini et al. since Pestka et al. uses the **natural** response of the cell to detect signaling. Without a reasonable expectation of success, a *prima facie* case of obviousness cannot be established.

Reconsideration and withdrawal of the obviousness rejections of claims 7 and 8 are requested.

Claim 9

Claim 9 stands rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Pestka et al. in view of Trueheart et al., and further in view of Mizushima et al. Applicants respectfully traverse the rejections.

Since dependent claim 9 includes the elements of independent claim 1 and a *prima facie* case of obviousness cannot be established with regard to independent claim 1, a *prima facie* case of obviousness also cannot be established with regard to dependent claim 9.

Reconsideration and withdrawal of the obviousness rejection of claim 9 is requested.

**Claim Objections**

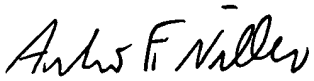
Claim 18 is objected to as assertedly being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claim 18 has been amended to further limit the subject matter of independent claim 15. Withdrawal of the objection is requested.

## REMARKS

In view of the foregoing amendments and remarks, applicants respectfully submit that the claims define patentable subject matter and an early notice of allowance is therefore solicited. Should questions remain after consideration of the foregoing, the Office is kindly requested to contact the applicants' attorney at the address or telephone number given herein.

Respectfully submitted,



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